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Originally published at:
Holz-Sapra, E; Glanzmann, C; Schmid, S; Went, P; Studer, G (2014). Lymphoepithelial carcinoma of the salivary glands: case report of a rare cancer and review of the literature. Journal of Medical Research and Development, 3(4):184-192.

Lymphoepithelial Carcinoma of the Salivary Glands: Case Report of a Rare Cancer and Review of the Literature

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Abstract-**Objective: Lymphoepithelial carcinoma (LEC) of the salivary glands is a very rare condition especially in the Caucasian population. We herewith contribute a case of a Caucasian woman with LEC of the parotid gland. Furthermore we present a literature review on LEC of the major salivary glands (MSG) of the past 32 years.**

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Review: We found 404 cases with LEC of the MSG published in 33 articles over the last 32 years. The mean age of the patients was 49 years (16-86); 56% were female. 95% of the cases have been treated and published in Asia (China, Taiwan). Only 17 of the 404 cases (4%) reported in 15 publications, Caucasian patients were affected. Information on treatment and outcome was not available in 75% and 72%, respectively. After a mean FU of 5.5 years (range 0.5-14) 66 of 84 (79%) patients with reported FU showed no evidence of disease.

Conclusion: LEC of the salivary glands is a rare disease especially in Caucasian populations with only 4% of published LEC cases in the reviewed literature. In only 21% of the reports, clinical information on treatment and outcome was provided. Based on the limited information available from published reports, the value of radiotherapy remains unclear.

Keywords- Lymphoepithelial Carcinoma, salivary Gland, Caucasian, Radiotherapy LEC, Outcome LEC

I INTRODUCTION

Lymphoepithelial carcinoma (LEC) of the salivary glands is a very rare finding especially in Europe. It accounts for approximately 0.4% of malignant salivary gland tumors [1].

Salivary glands tumors are in general uncommon accounting for less than 3% of all head and neck tumors. About 25 % of all tumors of the parotid glands are malignant [2]. In the world, the annual incidence of malignant tumors of the parotid gland vary between slightly less than 2 and greater than 0.05 per 100000 [3]. The most common malignant salivary glands tumors include mucoepidermoid carcinoma and adenoid cystic carcinoma, which together comprise approximately one-half of all malignant salivary gland tumors [2].

LEC of the parotid glands has a strong racial prevalence being more common in Eskimos and among southeastern Chinese. Eskimo and Asian population have the greatest incidence of LEC [4]. The incidence of malignant tumors of the salivary glands in Greenland is described in a report of Cleary et al with 3.9% in males and 7.7% in females [5]. Over 90% of these tumors occur in the parotid gland, and > 90% are LEC.

In 1921 A. Schmincke [6] as well as Regaud and Reverench [7] independent from each other described the first time a nasopharyngeal neoplasm characterized by undifferentiated epithelial tumor cells surrounded by lymphoid stroma. In 1962 Hildermann introduced the term “Lymphoepithelial Carcinoma” (LEC) [8]. Subsequently, morphologically similar tumors were described at various primary sites such as lacrimal and salivary glands, tonsil, thymus, lung, breast, uterus, stomach, urinary bladder, breast, pancreas, renal pelvis, ureter, mandible, vagina, rectum, trachea, kidney and skin. LEC is a specific subtype of undifferentiated carcinoma [9] and shares histological features with nasopharyngeal carcinoma and benign lymphoepithelial lesion [10]. In the literature the LEC outside the nasopharynx is also called Lympho-epithelioma-like carcinoma. The World Health Organization (WHO) defines it as undifferentiated carcinoma with lymphoid stroma [11].

In general, LEC may or may not be associated with Epstein-Barr virus (EBV) [12, 13]. There has been described a case of a LEC arising from a gland in which a benign lymphoepithelial lesion had been diagnosed before [14]. This might implicate a malignant transformation, but most LECs are not diagnosed on the background of a benign lymphoepithelial lesion and probably develop de novo [1]. LEC associated with EBV infection has been described in endemic areas such as Southeast Asia [12].

We report a case of LEC of the parotid gland to contribute to the limited case reports of this very rare tumor occurring to Caucasians. Furthermore, we performed a systematic review of the English literature of LECs of the MSGs from the last 32 years.

II MATERIALS AND METHODS

We reported one case of LEC diagnosed in the left parotid gland. Furthermore, we performed a systematic review of the English literature using MEDLINE (January 1980 – March 2013) and searched cross links manually. We included case series as well as case reports of LEC of the major salivary glands. Non-English publications and publications in abstract form only were excluded. Furthermore we excluded case series of LEC of head and neck if no details were provided for LEC of MSG. TN stage, age, gender, performed treatment and outcome have been assessed.

III STATISTICS

The Excel program was used as data basis and for statistical calculations, including mean, median and data range values. P values <0.05 were considered statistically significant, however, for this descriptive analysis no statistical calculations were required.

IV CASE PRESENTATION

A 28-year old woman presented with a swollen lymphatic node of the left side level II of the neck. Her medical history was not contributory. A fine needle aspiration cytology was carried out and showed the histopathological diagnosis of a LEC. The patient underwent a left complete parotidectomy and left modified neck dissection level II-IV, and a reconstruction of the ramus colli N. facialis with N. auricularis – transplant performed by an ENT surgeon (SS). The diagnosis of a LEC from the fine needle aspiration was confirmed by a second pathologist (Figs. 1 & 2). The lesion showed a diameter of 12 mm. The evidence of EBV was positive. In 13 of 49 lymphatic nodes cancer cells were detected. Most of lymph node metastases were located caudally of the parotid gland in level II. The maximum size of the clinically evident lymphatic node located in level II was 1.9 cm. There was no sign of extracapsular extension (ECE). The resection margin was locally less than 1 mm.

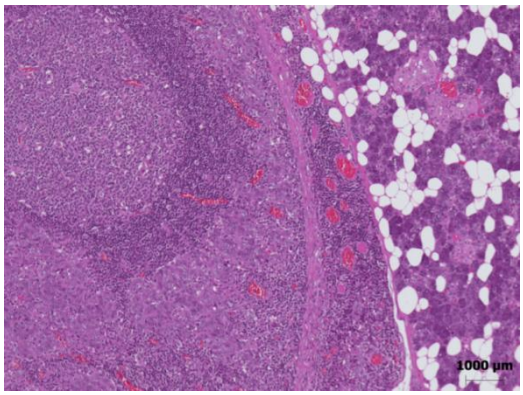

Fig. 1 Lymphoepithelial carcinoma tissue adjacent the glandula parotis. The overview depicts a dense lymphocytic tissue, which could obscure the tumor infiltration as seen in the lower left side of the figure. Germinal centers are frequently seen. No inflammatory infiltrates are seen in the normal parotid gland (HE Staining, x5)

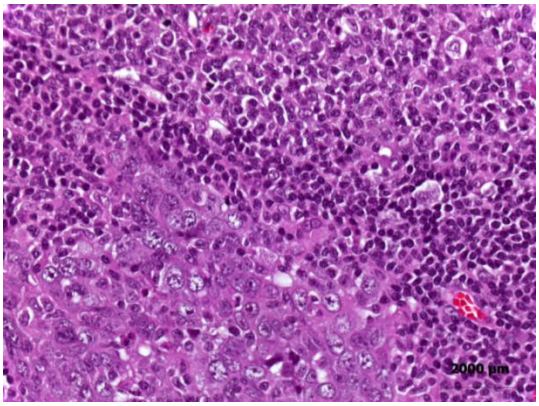

Fig. 2 Detailed morphology of the tumor. Syncytial infiltrating tumor cells are large and vesicular with prominent nucleoli. Small intratumoral lymphocytes and larger centroblasts are both significantly smaller if compared to the tumor cells (HE staining, x40)

The patient was referred to our clinic for post-operative radiation therapy. The planning target volume (PTV) to be covered was extensively discussed because of some uncertainty whether the lesion in the parotid gland representing a primary of the parotid gland or an intraparotideal lymph node metastases of an undetected nasopharyngeal primary (NPC). Regarding the fact that metastases of a NPC in the parotid gland is rather unusual [15], and that endoscopic as well as radiological evaluation (MRI and PET-CT) did not show any abnormal findings in the nasopharynx the lesion was considered as a primary of the parotid gland, TN stage pT3 pN2b (13/49) M0. A biopsy of the nasopharynx was not performed. A fine needle aspiration of a slightly enlarged lymphatic node of the contralateral side showed no tumor. The patient was treated with 4 dose levels (70, 66, 60 and 54 Gy) with stereotactic integrated boost (SIB) IMRT: 66 Gy in 2 Gy to the affected lymph nodes level II and III left side (Fig. 3), 54 Gy to elective lymph nodes level IV and V. A small boost of 70 Gy in 2.11 Gy per session (PTV: 7.4 cm³) was applied to a suspect macroscopic finding (Fig. 4) in the former tumor region. A margin of 1 cm (> .5cm – 2cm, depending on anatomical structures involved) around the GTV is used as PTV considering anatomic borders like bony structures.

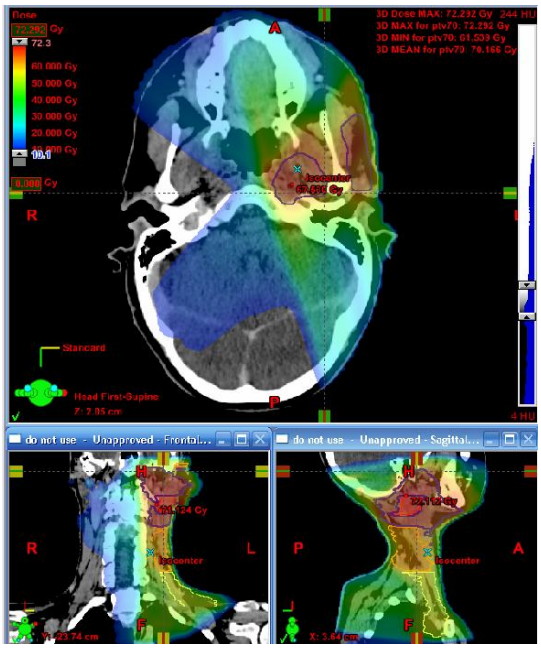

Fig. 3 Overview of 4 dose levels (70, 66, 60 and 54 Gy) with stereotactic integrated boost (SIB) IMRT

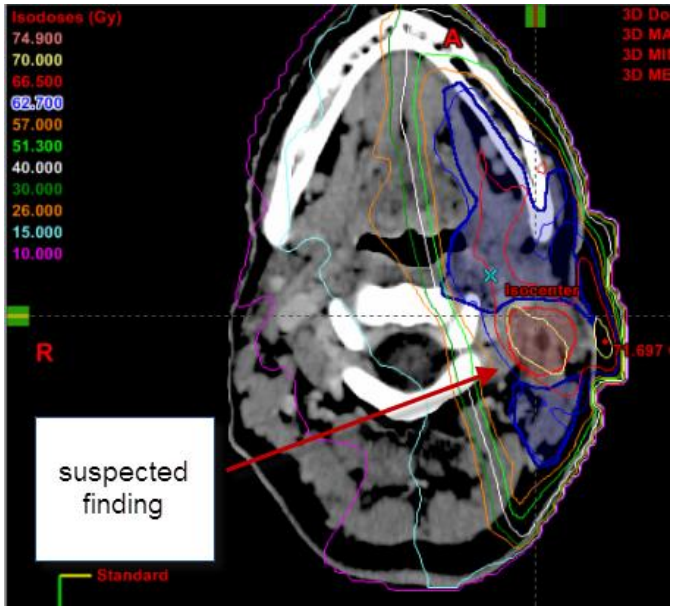

Fig. 4 suspect macroscopic finding in the former tumor region

A concomitant chemotherapy of carboplatin (4 cycles of 90 mg each) was administered. Cisplatin was stopped after one application of 40mg/m2/week because of tinnitus.

After radiochemotherapy, chemotherapy was administered according to the scheme of Al Sarraf [16] but using carboplatin instead of cisplatin considering the risk of a recurrent tinnitus. (3 cycles carboplatin AUC 6, absolute 750 mg day 1 und 5-FU 1'000 mg/m² per day, absolute 7'200 mg iv. day 1-5).

The chemoradiotherapy was tolerated very well by the patient besides the expected dysgeusia, odynophagia (RTOG grade II) and mucositis (RTOG grade II). During the adjuvant chemotherapy besides a moderate nausea, a thrombopenia (RTOG grade III) and leukopenia occurred (RTOG grade II).

The patient remained under regular FU including physical examinations and diagnostic imaging. The latest MRI (43 months after end of treatment) of the head and neck was bland. Meanwhile 5 years after the completion of treatment, the patient is alive with no evidence of disease (ANED) and no late toxicity.

V RESULTS OF THE LITERATURE REVIEW ON LEC OF MSG

33 publications met our criteria [9, 17-43].

Overall we found 404 cases of LEC (excluding our own case) in the salivary glands which have been published over the past 32 years: in 323/404 cases (80%), the primary was diagnosed in the parotid gland in 54 cases (13%) in the submandibular and in 27 cases (7%) in minor salivary glands. In only 18/405 cases (5%), own case included, Caucasians were affected, please see Tables 1 and 2.

TABLE 1 SUMMARY OF ALL PATIENTS AND TUMORS CHARACTERISTICS.

N publications	Author [ref]	year	n	n.caucasian	age (mean)	gender (f:m)	site	size (cm) Diameter, mean	T-status	N	EBV	Tx	FU (months, mean)	outcome
1	Redondo C. et al	1981	1	1	35	m	PG	2	na	N+	na	S	20	AD
2	Nagao et al.	1983	2	0	40	f	PG	4	na	na	na	S + RT	19	NED
3	Amaral AL et al	1984	1	1	86	f	SMG	5	na	N+	na	S (RT rejected)	29	NED
4	H M. Yazdi et al	1984	1	0	57	f	SMG	1.2	na	N+	na	S + RT	74	NED
5	E.K. Kott et al	1984	3	2	46	2:1	PG	6	na	na	na	S + RT	70	NED
6	Saw D. et al.	1988	8	0	49	3:5	PG 4, SMG 4	5	na	N0 7, N+ 1	6+, 2-	S + RT	17	NED 7, DUD 1 DOD 2, NED 3
7	Bosch JO et al.	1988	7	0	39	2:5	PG	na	na	na	na	S 3, S+RT 4	69	DUD 1, AD 1
8	Hamilton-Dutoit SJ et al.	1991	13	2	53	5:8	PG 9, SMG 4	na	na	na	12+, 1-	na	na	na
9	Lamer AP et al.	1991	6	1	55	4:2	PG 5, SMG 1	na	na	N0 2, na 4	6+	S 1, RT 1, S+RT 4	132	NED 4, DOD 2.
10	Borg MF et al.	1993	1	1	26	m	PG	na	na	N+	na	S + RT	na	NED
11	Chan John K.C. et al	1994	5	0	47	2:3	PG 1, SMG 4	na	na	na	4+ 1 na	S 1, S + RT 4	168	NED 4, na 1
12	Kountakis SE et al.	1995	2	2	62	f	PG	4	na	N0 1, N+ 1	-	S + RT	24	NED
13	Leung	1995	10	0	43	3:7	PG 8, SMG 2	na	2T1, 4 T2 1 T3, 1 T4, 2na	N+ 3, N0 5, na 2	4+, 6-	S + RT 8, na 2	43	DOD 1, na 2, AD 2, NED 5
14	Kotsianti A	1996	1	1	64	m	PG	5	na	N+	+	S	na	na
15	Tsai	1996	7	0	41	3:4	PG 6, SMG 1	na	na	N+ 4, N0 3	7+	S + RT 6, S 1	76	DOD 1, NED 6
16	Abdulla AK et al.	1996	1	0	58	m	PG	3	na	N0	+	S	24	AD, N+
17	Se-Jin Jang et al	1997	1	0	16	f	SMG	2.8	na	N0	+	S	10	NED
18	N. Knight Wordley et al.	1997	1	1	69	f	MSG	2	na	N0	na	S + RT	n.a	na
19	Wu DL et al.	2001	1	1	54	f	PG	4	na	N+	+	S + RT	24	NED
20	Bialas M et al.	2002	1	1	74	f	PG	5	na	N0	+	S + RT	na	na
21	Saku T et al.	2003	160	0	44	1:1:1	PG 112, SMG 23, MSG 25	na	na	na N+ 6	+	na	na	na
22	Cheng-Ping Wang et al.	2004	16	0	45	10:6	PG 15, SMG 1	4	T2-3	N0 5, na 5	+	S + RT 14, S 2	119	NED 14, DOD 2
23	Milena Saqui-Salces et al	2006	2	0	42	f	PG	9	na	N0 1, N+ 1	+	S + RT, S + CT	96	NED 1, DOD 1
24	Hermann Herbst et al.	2006	2	2	55	1:1	PG 1, SMG 1 PG 4	4	pT2, pT1	N0 1, N+ 1	+	S	n.a	na
25	C-Y Hsung et al	2006	8	0	43	5:3	SMG 3, MSG 1	na	T1-T4	N0 3, N+ 5	na	S + RT 7, S 1	69	NED 5, DOD 2, AD 1
26	A. Manganaris et al.	2007	1	1	67	f	PG	6	na	N0	+	S + RT	12	NED
27	Soumaya Ben Abdelkrim	2009	1	0	70	f	PG	7	na	N0	-	SG (RT not available)	5	NED
28	Tian et al.	2010	106	0	na	19:1	PG	na	na	na	na	na	na	na
29	Christopher G Tang et al	2012	1	0	29	f	PG	4	na	N0	+	S + RT	na	na
30	Sarika Gupta et al.	2012	1	0	40	f	PG	4	na	N0	+	S	na	na
31	Chelva R Spencer et al	2012	1	0	27	f	PG	na	na	na	+	S+ RCT	still under treatment	na
32	Friborg J. et al	2012	4	0	54	1:1	PG 2, SMG 2	na	na	na	+	S + RT: 3, S: 1	42 (2 na)	NED: 2
33	Wang YL et al	2012	28	0	na	na	PG 22, SMG 6	na	na	na	na	na	na	na
34	Holz et al.	2013	1	1	32	f	PG	1	pT3	N+	+	S + RCT	60	NED
Total Nulid = 405 (100%)			405	18	49 (16-86)	6:5	PG: 323 (80%) SMG: 56 (14%) MSG 27 (7%)	4 (1-9)	T1: 5% T2: 15 (40%) T3: 12 (32%) T4: 3 (8%)	N0: 56 (55%) N+: 29 (45%)	EBV+: 233 (95%) EBV-: 13 (5%)	S: 17 (15%) S + RT: 77 (77%) S + RCT:2 (2%) RT only:1 (1%) S + CT:1 (1%)	55 (6-168)	NED: 66 (78%) AD: 3 (11%) DUD: 1 (1%) DOD: 11 (13%)
					66%	93%	100%	12%	12%	17%	66%	23%	21%	21%

NA = not assessed, RT = radiotherapy, S = surgery, Ned = no evidence of disease, DUD, died of unrelated disease, DOD = died of disease, AD = alive with disease, PG = parotid gland, SMG = submandibular gland, MSG = minor salivary gland

TABLE 2 SUMMARY OF THE PATIENTS WITH CAUCASIAN ORIGIN ONLY

N	Author [ref]	year	n LEC cases	n caucasian	age (mean)	gender (f:m)	site	tumor size (cm) Diameter, mean	T	N	EBV	Therapy	FU (months, mean)	outcome
			35	18	54	2:1	PG:15 SMG:2 MSG:1	4	pT1:1 pT2:1 pT3:1	N+: 8 N0: 5	pos:8 neg:4	S: 5 S + RT: 10 S + RCT: 1	46	NED: 10 AD: 1
1	Redondo C. et al.	1981	1	1	35	m	PG	2	na	N+	na	S	20	AD
2	Amaral AL et al.	1984	1	1	86	f	SMG	5	na	N+	na	S (RT rejected)	29	NED
3	E K. Kott et al	1984	3	2	46	1:1	PG	6	na	na	na	S + RT	70	NED
4	Lanier AP et al.	1991	6	1	55	f	PG	na	na	na	pos.	S + RT	132	NED
5	Hamilton-Dutoit SJ e	1991	13	2	53	1:1	PG	na	na	na	neg	na	na	na
6	Borg MF et al.	1993	1	1	26	m	PG	na	na	N+	na	S + RT	na	NED
7	Kountakis SE et al.	1995	2	2	62	f	PG	4	na	N0 1 N+ 1	neg	S + RT	24	NED
8	Kotsianti A	1996	1	1	64	m	PG	5	na	N+	pos.	S	na	na
9	N. Knight Worley et	1997	1	1	69	f	MSG	2	na	N0	na	S + RT	na	na
10	Wu DL et al.	2001	1	1	54	f	PG	4	na	N+	pos.	S + RT	24	NED
11	Bialas M et al	2002	1	1	74	f	PG	5	na	N0	pos.	S + RT	na	na
12	Hermann Herbst et a	2006	2	2	55	1:1	PG 1, SMG 1	4	pT1 pT2	N0:1 N+:1	pos.	S	na	na
13	A. Manganaris et al.	2007	1	1	67	f	PG	6	na	N0	pos.	S + RT	12	NED
14	Holz et al.	2013	1	1	32	f	PG	1	pT3	N+	pos.	S + RCT	60	NED
available information in n= 18 (100%)					100	100	100	79%	16%	72%	66%	90%	50%	61%

VI DISCUSSION

We added a case of a LEC in an MSG to 404 cases found in a review of the English literature.

To our knowledge it is the first literature review focusing on LEC of the MSG. We found only 18 patients out of 405 with Caucasian origin (5%).

As many of the 33 reports were focused on histopathological features of the entity, clinical information turned out very limited. In only 21 % of the 33 reports (84 cases), clinical information on the treatment and outcome were available. The 2 publications with the most patients (Saku et al., Tian et al.) are from Asian countries and did not provide the required clinical information to estimate the potential value of postoperative radiation.

In the literature, a slight prevalence of the LEC has been suggested for the female sex [35] which is presented as well in our patients of Caucasian origin; 12/18 patients are female (66%). The publication of Saku et al (n =160) could not show a female predominance, therefore Tian et al (n= 106) published female cases twice as many as male cases.

Based on the reported provided details, only our own patient was treated trimodally with postoperative radio chemotherapy.

It has been supposed that LEC even outside the nasopharynx is a radiosensitive disease [44]. Dubey et al at M.D. Anderson have published a retrospective review of 34 patients from 1950-1994 with nonnasopharyngeal LEC of the head and neck. In 2 of these patients the primary tumor site was the parotid gland, no further details for these 2 two cases were provided. The local control rate of this series was 94% after a median FU of 7.5 years, so the authors suggested irradiation of the primary tumor of patients with nonnasopharyngeal LEC of the head and neck.

The knowledge about LEC is mainly based on numerous literature of nasopharyngeal cancer. Wolff et al showed in 6 patients with LEC of the nasopharynx in patients treated with primary radio chemotherapy followed by adjuvant administration of interferon-beta for 6 months a 100 percent OS after FU of 5 years [45]. Buehrlen et al demonstrated a cure rate >90 % in 45 patients (age 8-20 years) after treatment with primary radio chemotherapy (60 Gy) and adjuvant interferon-beta [46].

Based on the available data, the question of whether or not it is appropriate to treat a patient with LEC of the parotid glands like a patient with LEC of the nasopharynx remains open.

Based on the limited clinical data available, the value of additional postoperative radiation therapy in LEC of the salivary glands remains unclear.

VII CONCLUSIONS

Based on the limited information available of the published reports the value of radiotherapy for patients with LEC of the parotid gland remains unclear.

REFERENCES

[1] M. Schneider and C. Rizzardi, "Lymphoepithelial carcinoma of the parotid glands and its relationship with benign lymphoepithelial lesions," Arch Pathol Lab Med, vol. 132, pp. 278-82, 2008.

[2] M. Guzzo, L. D. Locati, F. J. Prott, G. Gatta, M. McGurk, and L. Licitra, "Major and minor salivary gland tumors," Crit Rev Oncol Hematol,vol. 2010;74:134-48.

[3] Cancer incidence in five continents, Volume VIII, IARC Sci Publ., pp. 1-781, 2002.

[4] S. J. Hamilton-Dutoit, M. H. Therkildsen, N. H. Neilsen, H. Jensen, J. P. Hansen, and G. Pallesen, "Undifferentiated carcinoma of the salivary gland in Greenlandic Eskimos: demonstration of Epstein-Barr virus DNA by in situ nucleic acid hybridization," Hum Pathol., vol. 22, pp. 811-815, 1991.

[5] K. R. Cleary and J. G.Batsakis, "Undifferentiated carcinoma with lymphoid stroma of the major salivary glands," Ann Otol Rhinol Laryngol, vol. 99, pp. 236-238, 1990.

[6] A. Schmincke, "Über lympho-epitheliale Geschwülste," Beitr Pathol Anat Allg Pathol, vol. 68, pp. 161-70, 1921.

[7] Foray N. Claudius Regaud (1870–1940): relecture des archives d'un pionnier de la radiobiologie et de la radiothérapie, Cancer/Radiothérapie, vol. 16, pp. 315-21, 2012.

[8] H. zur Hausen, H. Schulte-Holthausen, and G. Klein, et al., "EBV DNA in biopsies of Burkitt tumours and anaplastic carcinomas of the nasopharynx," Nature, vol. 228, pp. 1056-8, 1970.

[9] C. P. Wang, Y. L. Chang, J. Y. Ko, P. J. Lou, C. F. Yeh, and T. S. Sheen, "Lymphoepithelial carcinoma versus large cell undifferentiated carcinoma of the major salivary glands," Cancer, vol. 101, pp. 2020-7, 2004.

[10] G. Jayaram and S. C. Peh, "Lymphoepithelial carcinoma of salivary gland - cytologic, histologic, immunocytochemical, and in situ hybridization features in a case," Diagn Cytopathol, vol. 22, pp. 400-2, 2000.

[11] G. Seifert and L. H. Sobin, "The World Health Organization's Histological Classification of Salivary Gland Tumors. A commentary on the second edition," Cancer, vol. 70, pp. 379-85, 19992.

[12] J. Sckolnick, J. Murphy, and J. L. Hunt, "Microsatellite instability in nasopharyngeal and lymphoepithelial carcinomas of the head and neck," Am J Surg Pathol., vol. 30, pp. 1250-1253, 2006.

[13] D. Rades, M. Stoehr, and T. Meyners, et al., "Evaluation of prognostic factors and two radiation techniques in patients treated with surgery followed by radio(chemo)therapy or definitive radio(chemo)therapy for locally advanced head-and-neck cancer," Strahlenther Onkol, vol. 184, pp. 198-205, 2008.

[14] G. L. Ellis PLA, Tumors of the Salivary Glands, Atlas of Tumor Pathology: Third Series, Fascicle 17, Washington D.C., 1996.

[15] VF-H. Chong, and Y-F. Fan, "Parotid Gland Involvement in Nasopharyngeal Carcinoma," Journal of Computer Assisted Tomography, vol. 23, pp. 524-8, 1999.

[16] M. Al-Sarraf, M. LeBlanc, and P. G. Giri, et al., "Chemoradiotherapy versus radiotherapy in patients with advanced nasopharyngeal cancer: phase III randomized Intergroup study 0099," J Clin Oncol., vol. 16, pp. 1310-7, 1998.

[17] T. Saku, J. Cheng, and K. Y. Jen, et al., "Epstein-Barr virus infected lymphoepithelial carcinomas of the salivary gland in the Russia-Asia area: a clinicopathologic study of 160 cases," Arkh Patol, vol. 65, pp. 35-9, 2003.

[18] Z. Tian, L. Li, L. Wang, Y. Hu, and J. Li, "Salivary gland neoplasms in oral and maxillofacial regions: a 23-year retrospective study of 6982 cases in an eastern Chinese population," Int J Oral Maxillofac Surg, vol. 39, pp. 235-42, 2010.

[19] C. Redondo, A. Garcia, and F. Vazquez, "Malignant lymphoepithelial lesion of the parotid gland: poorly differentiated squamous cell carcinoma with lymphoid stroma," Cancer, vol. 48, pp. 289-92, 1981.

[20] J. D. Bosch, W. H. Kudryk, and G. H. Johnson, "The malignant lymphoepithelial lesion of the salivary glands," J Otolaryngol, vol. 17, pp. 187-90, 1988.

[21] K. Nagao, O. Matsuzaki, and H. Saiga, et al., "A histopathologic study of benign and malignant lymphoepithelial lesions of the parotid gland," Cancer, vol. 52, pp. 1044-52, 1983.

[22] A. L. Amaral and A. G. Nascimento. "Malignant lymphoepithelial lesion of the submandibular gland," Oral Surg Oral Med Oral Pathol, vol. 58, pp. 184-90, 1984.

[23] H. M. Yazdi and G. R. Hogg, "Malignant lymphoepithelial lesion of the submandibular salivary gland," Am J Clin Pathol, vol. 82, pp. 344-8, 1984.

[24] Kott ET, Goepfert H, Ayala AG, Ordonez NG. "Lymphoepithelial carcinoma (malignant lymphoepithelial lesion) of the salivary glands," Arch Otolaryngol 1984;110:50-3.

[25] D. Saw, W. H. Lau, J. H. Ho, J. K. Chan, and C. S. Ng, "Malignant lymphoepithelial lesion of the salivary gland," Hum Pathol, vol. 17, pp. 914-23, 1986.

[26] A. P. Lanier, S. R. Clift, G. Bornkamm, W. Henle, H. Goepfert, and N. Raab-Traub, "Epstein-Barr virus and malignant lymphoepithelial lesions of the salivary gland," Arctic Med Res, vol. 50, pp. 55-61, 1991.

[27] S. Y. Leung, L. P. Chung, S. T. Yuen, C. M. Ho, M. P. Wong, and S. Y. Chan, "Lymphoepithelial carcinoma of the salivary gland: in situ detection of Epstein-Barr virus," J Clin Pathol, vol. 48, pp. 1022-7, 1995.

[28] C. C. Tsai, C. L. Chen, and H. C.Hsu, "Expression of Epstein-Barr virus in carcinomas of major salivary glands: a strong association with lymphoepithelioma-like carcinoma," Hum Pathol, vol. 27, pp. 258-62, 1996.

[29] J. K. Chan, T. T. Yip, W. Y. Tsang, Y. F. Poon, C. S. Wong, V. W. Ma, "Specific association of Epstein-Barr virus with lymphoepithelial carcinoma among tumors and tumorlike lesions of the salivary gland," Arch Pathol Lab Med, vol. 118, pp. 994-7, 1994.

[30] S. E. Kountakis, W. SooHoo, and A. Maillard, "Lymphoepithelial carcinoma of the parotid gland," Head Neck , vol. 17, pp. 445-50, 1995.

[31] A. K. Abdulla and M. Y. Mian, "Lymphoepithelial carcinoma of salivary glands," Head Neck, vol. 18, pp. 577-81, 1996.

[32] A. Kotsianti, J. Costopoulos, S. Morgello, C. Papadimitriou, "Undifferentiated carcinoma of the parotid gland in a white patient: detection of Epstein-Barr virus by in situ hybridization," Hum Pathol, vol. 27, pp. 87-90, 1996.

[33] N. K. Worley and P. J. Daroca, Jr. "Lymphoepithelial carcinoma of the minor salivary gland," Arch Otolaryngol Head Neck Surg., vol. 123, pp. 638-40, 1997.

[34] S. J. Jang, S. S. Paik, and W. M. Lee, et al., "Lymphoepithelial carcinoma of the submandibular gland--a case report," J Korean Med Sci., vol. 12, pp. 252-5, 1997.

[35] D. L. Wu, L. Shemen, T. Brady, and D. Saw, "Malignant lymphoepithelial lesion of the parotid gland: a case report and review of the literature," Ear Nose Throat J., vol. 80, pp. 803-6, 2001.

[36] H. Herbst and G. Niedobitek, "Sporadic EBV-associated lymphoepithelial salivary gland carcinoma with EBV-positive low-grade myoepithelial component," Virchows Arch., vol. 448, pp. 648-54, 2006.

[37] C. Y. Hsiung, C. C. Huang, C. J. Wang, E. Y. Huang, and H. Y. Huang, "Lymphoepithelioma-like carcinoma of salivary glands: treatment results and failure patterns," Br J Radiol., vol. 79, pp. 52-5, 2006.

[38] A. Manganaris, F. Patakiouta, P. Xirou, and T. Manganaris, "Lymphoepithelial carcinoma of the parotid gland: is an association with Epstein-Barr virus possible in non-endemic areas," Int J Oral Maxillofac Surg., vol. 36, pp. 556-9, 2007.

[39] M. Saqui-Salces, B. Martinez-Benitez, and A. Gamboa-Dominguez, "EBV+ lymphoepithelial carcinoma of the parotid gland in Mexican Mestizo patients with chronic autoimmune diseases," Pathol Oncol Res., vol. 12, pp. 41-5, 2006.

[40] S. B. Abdelkrim, A. Trabelsi, and F. Hammedi, et al., "Primary lymphoepithelial carcinoma of the parotid gland in a North African woman," Rare Tumors, vol. 1, p. 16, 2009.

[41] C. G. Tang, C. G. Schmidtknechtx, G. Y. Tang, L. J. Schloegel, and B. Rasgon "Lymphoepithelial carcinoma: a case of a rare parotid gland tumor," Perm J., vol. 16, pp. 60-2, 2012.

[42] S. Gupta, K. S. Loh, and F. Petersson, "Lymphoepithelial carcinoma of the parotid gland arising in an intraglandular lymph node: report of a rare case mimicking metastasis," Ann Diagn Pathol, vol. 16, pp. 416-21, 2012.

[43] Y. L. Wang, Y. X. Zhu, T. Z. Chen, and et al., "Clinicopathologic study of 1176 salivary gland tumors in a Chinese population: experience of one cancer center 1997-2007," Acta Otolaryngol, vol. 132, pp. 879-86, 2012.

[44] P. Dubey, C. S. Ha, and K. K. Ang, et al., "Nonnasopharyngeal lymphoepithelioma of the head and neck," Cancer, vol. 82, pp. 1556-62, 1998.

[45] H. A. Wolff, R. M. Rodel, B. Gunawan, and et al. "Nasopharyngeal carcinoma in adults: treatment results after long-term follow-up with special reference to adjuvant interferon-beta in undifferentiated carcinomas," J Cancer Res Clin Oncol, vol. 136, pp. 89-97, 2010.

[46] M. Buehrlen, C. M. Zwaan, and B. Granzen, et al. "Multimodal treatment, including interferon beta, of nasopharyngeal carcinoma in children and young adults: preliminary results from the prospective, multicenter study NPC-2003-GPOH/DCOG," Cancer, vol. 118, pp. 4892-900, 2012.